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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,849	02/07/2002	John Lyons	12636-260	1393

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EXAMINER	
KHARE, DEVESH	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/25/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,849	LYONS, JOHN	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1-42 and 52-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *5* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 52-56, drawn to a composition comprising a cytidine analog and imatinib mesylate, classified in class 536 and 424, subclass various.

II. Claims 1-30, 57 and 58, drawn to a method for treating chronic myelogenous leukemia (CML) with a DNA methylation inhibitor (cytidine analog), classified in classes 514, subclass various.

III. Claims 31-42, drawn to a method of treating CML with imatinib mesylate and decitabine (5-azacytidine) such that the patient's resistance to imatinib mesylate in the absence of decitabine is reduced, classified in class 514, subclass various.

IV. Claims 43-51, drawn to a method of treating CML with a DNA methylation inhibitor in combination with imatinib mesylate, classified in class 514, subclass various.

The inventions are distinct, each from the other because of the following reasons: Groups I and II-IV are related as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for making the product as claimed can be practiced with another materially different process or (2) the product as claimed can be made in a materially different process of making that product (MPEP § 806.05(h)). In the instant case the claims are drawn to a

methods for treating CML, indicating that the product (the composition of Group I) can be used by a materially different method.

Inventions II/III, II/IV and III/IV are unrelated to one another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01).

Group II is drawn to a method for treating chronic myelogenous leukemia (CML) with a DNA methylation inhibitor, which is unrelated to a method of treating CML with imatinib mesylate and decitabine (5-azacytidine) such that the patient's resistance to imatinib mesylate in the absence of decitabine is reduced, of Group III.

Group II is drawn to a method for treating chronic myelogenous leukemia (CML) with a DNA methylation inhibitor, which is unrelated to a method of treating CML with a DNA methylation inhibitor in combination with imatinib mesylate, of Group IV.

Group III is drawn to a method of treating CML with imatinib mesylate and decitabine (5-azacytidine) such that the patient's resistance to imatinib mesylate in the absence of decitabine is reduced, which is unrelated to a method of treating CML with a DNA methylation inhibitor in combination with imatinib mesylate, of Group IV.

Although the inventions are classified in the same class and sub-class, searching the four groups of inventions constitutes a burdensome search, as a thorough search comprises a search or foreign patents and non-patent literature as well as the appropriate U.S. patent classifications. Because these inventions are distinct for the

reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper. It is noted that the four independent and distinct inventions would indeed impose an undue burden upon the examiner in charge of this application.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143). If applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. (MPEP § 821.04)

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

A telephone call was made to Shirley Chen on August 13, 2003 to request an oral election to the above restriction requirement. During telephone conversation with Shirley Chen on August 14, 2003 a provisional election was made without traverse to prosecute the invention of Group IV, claims 43-51. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-42 and 52-58 withdrawn from further

consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 43-51 are currently pending in this application.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

Claim 45 is rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is directed to method of determining a number of blasts, promyelocytes, basophil, and platelets per liter of peripheral blood or bone marrow, depends on the method claim 44, and is directed to a method for treating a patient having chronic myelogenous leukemia. The recitation in a dependent claim of "determining a number of

blasts" to be used in a method from which said claim depends, wherein "determining a number of blasts" does not result in a patentably distinguishable methodological and manipulative difference in how said determination of a number of blasts impacts the method from which it depends, renders the claim 45 indefinite for failing to distinctly articulate how such a recitation further limits the method of claim 44.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43-51 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Von Hoff et al. (Ann. Int. Med. 85(2) pages 237-45, 1976) in view of Kantarjian et al. (Conference: Blood 98 (11), Part 1, pp 141a, 2001).

Claims 43-51 are drawn to method for treating a patient having chronic myelogenous leukemia (CML), with a composition comprising a therapeutically effective amount of a DNA methylation inhibitor in combination with imatinib mesylate.

Additional claim limitations include more than 30% blasts in peripheral blood or bone marrow where the patient's CML is staged, DNA methylation inhibitor is a cytidine analog or decitabine (5-azacytidine), administration by intravenous infusion at a dose ranging between 1 to 100 mg/m^2.

Von Hoff et al. teach the use and effectiveness of 5-azacytidine, the cytidine analog, in the treatment of acute myelogenous leukemeia (abstract). Von Hoff et al. discloses the effectiveness of 5-azacytidine in childhood leukemia or during the induction phase (page 239, col. 2nd. under European Trials). It is noted that Von Hoff et al. do not provide specific disclosure where the patient's CML is staged prior to administration or the administration is performed when the patient is in blast phase of CML. Von Hoff et al. teach the administration of 5-azacytidine by intravenous and subcutaneous routes (page 239, first col. first para. lines 2-7). Von Hoff et al. also suggest the dosage of 5-azacytidine for intravenous administration in the ranges of 1.1- 633.0 mg/m^2 (page 239, table 1 and page 240, 2nd col. 2nd para.). Von Hoff et al. further teach the combination therapy of acute myelogenous leukemia with 5-azacytidine with other agents (page 241, table 3). Von Hoff et al. suggest a need for future clinical studies for using 5-azacytidine alone and in combination with other agents in the treatment of acute myelogenous leukemia (page 244, first col. third. para.).Von Hoff et al. differs from the applicant's invention that Von Hoff et al. do not provide an example of the administration of the pharmaceutical composition, comprising 5-azacytidine in combination with imatinib mesylate.

Kantarjian et al. teach the treatment of CML with imatinib mesylate (see abstract). Kantarjian et al. disclose the treatment of patients with CML with imatinib mesylate 400-600 mg/day (lines 1-2) for blasts 10-14% (lines 5-6). Kantarjian et al. also suggest a need for future clinical studies in CML treatment with imatinib mesylate in combination with decitabine (5-azacytidine) (see last two lines). It is noted that

Kantarjian et al. do not provide specific disclosures regarding the treatment of CML with both imatinib mesylate and the decitabine (5-azacytidine).

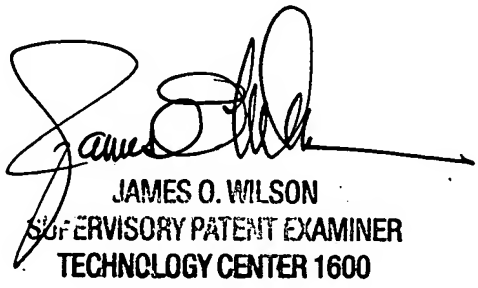
Therefore, one of ordinary skill in the art would have found the applicants claimed method for treating a patient having chronic myelogenous leukemia (CML), with a therapeutically effective amount of a 5-azacytidine (an analog of cytidine or a DNA methylation inhibitor) in combination with imatinib mesylate, to have been obvious at the time the invention was made having the above cited references before him. Since Von Hoff et al. teach the use and effectiveness of 5-azacytidine, in the treatment of acute myelogenous leukemeia, and Kantarjian et al. teach the treatment of CML with imatinib mesylate, one skilled in the art would have a reasonable expectation for success in combining the teachings of these references to accomplish the treatment of CML because both 5-azacytidine and imatinib mesylate have shown activity against resistant phase CML as single agents and were therefore tested in combination. The motivation for doing so is provided in the prior art, Kantarjian et al. suggest a need for future clinical studies in CML treatment with imatinib mesylate in combination with decitabine (5-azacytidine) (see last two lines).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is (703)605-

1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
August 22,2003